#8 Decl. 7/8/02

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In re Application of)
)
Fields *et al.*)
)
Serial No. 09/758,308)
)
Filed: January 10, 2001)
)
For: ANTIGENIC EPITOPES AND)
MOSAIC POLYPEPTIDES OF)
HEPATITIS C PROTEINS)

Group Art Unit: 1648

Examiner: Bao Qun Li

DECLARATION OF HOWARD A. FIELDS AND YURI KHUDYAKOV UNDER 37 C.F.R. § 1.131

Commissioner for Patents
Washington, D.C. 20231

NEEDLE & ROSENBERG, P.C.
The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811

June 26, 2002

Sir:

We, Howard A. Fields and Yuri E. Khudyakov declare the following:

1. We are the applicants of the above-identified patent application and co-inventors of the subject matter described and claimed therein.

2. Prior to the November 27, 1997 publication date of Valenzuela et al. (WO 97/44469), we had conceived of the invention described and claimed in claims 7-31 of the subject application in this country, and reduced the invention to practice, as evidenced by the following:

> CRADA between The Centers for Disease Control and Prevention (CDC) and Boehringer Mannheim GmbH (BMG) Appendix B prepared prior to November 27, 1997, wherein, when describing certain attributes of the invention, it describes "[a]nother advantage is the ability to connect in one polypeptide chain antigenic epitopes from different virus-specific proteins belonging to different viral strains." As described elsewhere in the provided document, examples of peptide sequences include those from "...HCV NS3-, NS4, and NS5-proteins..."

Because we were aware of a number of sequences that comprised epitopes of the proteins of the HCV polyprotein of different HCV strains, we envisioned the structure of a polypeptide chain containing epitopes of HCV-specific proteins from different viral strains.

3. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like are punishable by

ATTORNEY DOCKET NO. 14114.0349U2
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fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that any such false statement may jeopardize the validity of the application or any patent issued thereon.

Howard A. Fields — DATE 6/26/02

Yuri E. Khudyakov — DATE 6-26-02

cooperation will involve the development of various artificial recombinant proteins composed of broadly immunoreactive antigenic epitopes. The protein is called a "mosaic" protein because it is composed of a mosaic of antigenic epitopes.

II. Research Plan

A. HCV Mosaic Proteins as Diagnostic Reagents:

Recently, a new strategy for the construction of diagnostic reagents, designated as "mosaic proteins", has been developed in the Hepatitis Branch at the CDC. This strategy was applied to the construction of a mosaic protein composed of only antigenic epitopes from the structural proteins of the hepatitis E virus (Khudyakov et al., Artificial mosaic protein containing antigenic epitopes of the hepatitis E virus. J Virol.

mosaic proteins would also have utility especially in cases where neutralizing antigenic epitopes are, or predicted to be, found in broad sequence and

specificity variations such as in the human immunodeficiency virus and HCV. The project is devoted to constructing and evaluating mosaic proteins that contain HCV-specific antigenic epitopes useful as immunodiagnostic reagents for the development of diagnostic tests.

C. Diagnostic Test for the Discrimination of Recent and Late HCV Infections

Recently, using 150 synthetic peptides spanning the entire HCV NS3-, NS4-, NS5-proteins we have identified a large number of linear B-cell epitopes (Fields et al., in press; Khudyakov et al., submitted).